

Management of women with stage IB2 cervical cancer with treatments other than chemoradiotherapy: A summary of the evidence

Background

The international Federation of Gynaecology and Obstetrics (FIGO) categorises stage 1B2 cervical cancer as a clinically visible lesion >4cm in greatest dimension confined to the cervix.¹ Treatment options for stage 1B2 cervical cancer include: concurrent chemotherapy and radiotherapy (chemoradiotherapy) without surgery; primary surgery with or without adjuvant therapy; or neoadjuvant chemotherapy followed by surgery.

There are no Australian guidelines for the management of stage 1B2 cervical cancer, but in other international guidelines, concurrent chemoradiotherapy is most commonly recommended as the primary treatment.²⁻⁶ These recommendations are based on evidence such as that in a recent Cochrane review which reported that chemoradiotherapy is more effective than radiotherapy alone for women with cervical cancer.⁷ However, limited recommendations are available regarding alternative treatment options such as primary surgery or neoadjuvant chemotherapy. A summary of the evidence for these treatment options is provided below, based on a recent systematic review undertaken by Cancer Australia.⁸

Surgery

The systematic review of the effectiveness of surgery⁸ considered the evidence by four categories: surgery, trachelectomy, completion surgery (hysterectomy after radiotherapy/chemoradiotherapy), and different surgical methods for performing hysterectomy.

Fourteen studies, including one randomised controlled trial (RCT), investigated surgery compared to primary radiotherapy/chemotherapy, and found that patients with primary surgery may have improved survival than patients with radiotherapy/chemotherapy. However these results were inconsistent. Adverse events and recurrence were not statistically significant between groups, although recurrence appeared to be more common in patients undergoing radiotherapy. No fertility outcomes were reported in the comparative studies.

Three comparative studies investigating trachelectomy were identified. Of these studies, two were reported abstracts, therefore information was limited. No differences were reported between trachelectomy and hysterectomy for survival, recurrence, sexual dysfunction or quality of life. No fertility outcomes were reported in the comparative studies.

Seven studies (which included three RCTs) investigated the addition of hysterectomy following primary radiotherapy/chemoradiotherapy (completion surgery). Completion surgery did not have any significant survival benefits when compared to radiotherapy/chemotherapy alone. In addition completion surgery may reduce the risk of recurrence, although there were inconsistencies between studies. No major differences in adverse events between groups were reported. Quality of life and fertility outcomes were not reported in any of the completion surgery studies.

Thirty eight studies were identified comparing different methods for performing radical hysterectomy. From these studies, outcome data was presented from five systematic reviews and three RCTs. The most commonly reported comparisons were between open/abdominal radical hysterectomy, laparoscopic radical hysterectomy and, or robotic radical hysterectomy. The majority of studies reported no significant difference in surgical outcomes between robotic and laparoscopic hysterectomy. Some studies reported poorer surgical outcomes and higher rates of adverse events with open/abdominal radical hysterectomy compared to robotic hysterectomy.

Neoadjuvant chemotherapy

Forty studies were identified (four systematic reviews, 11 RCTs and 25 non-RCTs) and were divided into two categories: neoadjuvant chemotherapy followed by local treatment compared with local treatment alone (note local treatment was usually surgery) and comparisons of different neoadjuvant chemotherapy regimens. Outcome data was presented from three high quality systematic reviews and four RCTs that were not already included in these reviews.

Two studies reported no statistically significant differences between neoadjuvant chemotherapy and surgery groups, as well as inconsistent results for survival. Pooled results reported in two systematic reviews indicated no statistically significant difference between neoadjuvant chemotherapy and surgery in one and a survival benefit following neoadjuvant chemotherapy in the other. Tierney et al (2004) reported that neoadjuvant chemotherapy tended to improve survival in trials using chemotherapy cycle lengths shorter than 14 days or cisplatin dose intensities greater than 25 mg/m² per week. No statistically significant differences in rates of recurrence were reported between neoadjuvant chemotherapy and surgery groups.

Higher responses to neoadjuvant chemotherapy were observed with the three-drug combination (paclitaxel/ifosfamide/cisplatin (TIP)); however this was also associated with more toxicity than either two-drug combination ifosfamide/cisplatin (IP) or paclitaxel/cisplatin (TP). No quality of life data were reported.

Fertility preservation procedures

Thirteen studies were identified on fertility preservation in populations thought to include stage IB2 cervical cancer. No comparative studies were identified, only small case series and surveys. Two papers reported successful full term pregnancies following assisted conception after trachelectomy. Following surgery, women were often concerned about recurrence, health of any future babies and pressure to conceive. No papers were identified on fertility outcomes following ovarian transposition in populations including stage IB2 cervical cancer.

Ongoing trials

A number of RCTs are currently being conducted in the management of stage IB2 cervical cancer, particularly comparing primary surgery or neoadjuvant chemotherapy with concurrent chemoradiotherapy. Results of these trials, which are not expected to be completed before 2018, are awaited with interest.

Summary

The majority of international guidelines recommended concurrent chemoradiotherapy as the primary treatment for stage 1B2 cervical cancer (NCCN, ESMO, SIGN, ACR and CCO).²⁻⁶ The NCCN and NICE guidelines also discuss radical hysterectomy as an option for primary treatment.^{2, 9, 10} While NCCN does not recommend neoadjuvant chemotherapy,² ESMO note that neoadjuvant chemotherapy is an emerging area of investigation and appropriate indications have yet to be established.³ No guideline recommendations were provided regarding the use of completion surgery, the ACR noted this was an area of investigation,⁵ while the NCCN noted that the Panel disagreed regarding the use of completion surgery.²

Due to limitations with the evidence no assessment can be made regarding the relative effectiveness of primary surgery, or neoadjuvant chemotherapy followed by surgery, compared to chemoradiotherapy. Consequently, based on current available evidence it is difficult to determine if either primary surgery or neoadjuvant chemotherapy followed by surgery represent optimal treatment for stage 1B2 cervical cancer. Patient factors and patient/physician preference are likely to influence treatment choice. Results from ongoing trials and a planned Cochrane review of radical hysterectomy versus chemoradiotherapy as primary treatment for stage 1B2 cervical cancer¹¹ may further guide management of these patients.

References

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